

Table 1: HEPARANASE SEQUENCE HOMOLOGY DATA

	10	20	30	40	50	60
mouse	-MLR-----	L L L L W L W G P I G A L A Q G A P A G T A P T D D V V D L E F Y T K R P L R S V S P S F L S I T				
rat	-MLRP-----	L L L L W L W G R I R A L T Q G T P A G T A P T K D V V D L E F Y T K R L F Q S V S P S F L S I T				
human	MLLRSPALPPPLMLLLGPIGLSPGALPRPAQAQDVVDLDFFTQEPHLVSPSFLSVT					
chicken	MLVLLLVLLAVPP-----	RR-TAEQLGLREPIGAVSPAFLSLT				
	*: * *	*: * *	*: * *	*: * *	*: * *	*: * *
	70	80	90	100	110	120
mouse	IDASLATDPRFLTFLGS	PRLRALARGLSPAYLRFGGKTDFLI	FDPKKEPTS	EERSYWK		
rat	IDASLATDPRFLTFLGS	PRLRALARGLSPAYLRFGGKTDFLI	FDPKKEPTS	EERSYWK		
human	IDANLATDPRFLILIGS	PKLRTLARGLSPAYLRFGGKTDFLI	FDPKKEPTS	EERSYWK		
chicken	LDASLATDPRFVALLRH	PKLHTLASGLSPGLRFGGKTDFLI	FDPKKEPTS	EERSYWK		
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	130	140	150	160	170	180
mouse	QVNNDICRSEFVSAAVL	KKLQVEWPFQELLLRE	QYQKEFKNSTY	SRSSVDM	LYSFAKCS	
rat	QDNNDICGSEVSADVL	KKLQMEWPFQELLLRE	QYQKEFKNSTY	SRSSVDM	LYSFAKCS	
human	QVNQDICKYGSIPDVE	KKLRLWPYQELLLRE	QYQKEFKNSTY	SRSSVDM	LYTFAKCS	
chicken	QAK-DVCEAWPSFAVVP	KLTLQWPLQELLLA	HSWKHKNTT	TRSTLDI	LHTFASSS	
	*: * *	*: * *	*: * *	*: * *	*: * *	*: * *
	190	200	210	220	230	240
mouse	GLDLIFGLNALLRTPDL	RWNSSNAQLLDYCSS	KGYNISWELGNE	PNSFWKKAH	ILIDGL	
rat	RLDLIFGLNALLRTPDL	RWNSSNAQLLDYCSS	KGYNISWELGNE	PNSFWKKAH	ISIDGL	
human	GLDLIFGLNALLRTPDL	RWNSSNAQLLDYCSS	KGYNISWELGNE	PNSFWKKAH	IFIDGL	
chicken	GFRVFGNALLRRLAGL	QWSSNAQLLDYCSS	KGYNISWELGNE	PNSFWKKAH	ICIDGL	
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	250	260	270	280	290	300
mouse	QLGEDFVELHKL	QRS-AFQNAKLYGPD	IGQPRGKTVKLLRS	SFLKAGGEV	IDSLTWHHYY	
rat	QLGEDFVELHKL	QKS-AFQNAKLYGPD	IGQPRGKTVKLLRS	SFLKAGGEV	IDSLTWHHYY	
human	QLGEDYIQLHKL	LRKS-TFQNAKLYGPD	VGQPRKKTAKMLK	SFLKAGGEV	IDSVTWHHYY	
chicken	QLGRDFVHLRQL	LSQPLYPHAEYGLD	VGQPRKKTQHL	LSFMKSGGKA	IDSVTWHHYY	
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	310	320	330	340	350	360
mouse	LNGRIATKEDFLSSD	ALDTFILSVQKILKVT	KEITPGKKVWLGET	SSAYGGGAPL	LSNTF	
rat	LNGRVATKEDFLSSD	VLDTFILSVQKILKVT	KEITPGKKVWLGET	SSAYGGGAPL	LSNTF	
human	LNGRTATREDFLNP	DPVLDIFISSVQKVQV	VESTRPGKKVWLGET	SSAYGGGAPL	LSDTF	
chicken	VNGRSATREDFLSPE	VLDSFATAIHDLVGI	VEATVPGKKVWLGET	SSAYGGGAPL	QLSNTY	
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	370	380	390	400	410	420
mouse	AAGFMWLDKLGSLA	QMGIEVVMRQVFGAG	NYHLVDENFEPL	PDYWLSLLFKK	LVGPRVL	
rat	AAGFMWLDKLGSLA	QMGIEVVMRQVFGAG	NYHLVDENFEPL	PDYWLSLLFKK	LVGPKVL	
human	AAGFMWLDKLGSLA	RMGIEVVMRQVFGAG	NYHLVDENFEPL	PDYWLSLLFKK	LVGTVKL	
chicken	VAGFMWLDKLGSLA	ARRGIDVVMRQVFGAG	SVHLVDAGFKPL	PDYWLSLLYK	RLVGTAVL	
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	430	440	450	460	470	480
mouse	LSRVKGPDRSKLRV	YLHCTNYHPRYQEGD	LTYVLNLHNVTKH	LKVPPLFRKP	VDIYL	
rat	MSRVKGPDRSKLRV	YLHCTNYHPRYQEGD	LTYVLNLHNVTKH	LKLPPLPMF	SRPVDIYL	
human	MASVQGSRRRLRV	YLHCTNIDNPRYQEGD	LTYVLNLHNVTKY	LRLPYPSNK	QVDIYL	
chicken	QASVEQADARRRV	YLHCTNIDNPRYQEGD	VTFLALNLSNVTQS	LQLPKQLWSKS	VDIYL	
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	490	500	510	520	530	540
mouse	LKPSGPDGLLSKSV	QLNGQILKMDVDEQ	TLPAITEKPLPAGS	SALSPAFSYGFF	VIRNAKI	
rat	LKPSGPDGLLSKSV	QLNGQILKMDVDEQ	TLPAITEKPLPAGS	SALSPAFSYGFF	VIRNAKI	
human	LRPLGPHGLLSKSV	QLNGQILKMDVDEQ	TLPAITEKPLPAGS	SALSPAFSYGFF	VIRNAKI	
chicken	LLPHGKDSILSREV	QLNGRLQMDVDEQ	TLPAITEKPLPAGS	SALSPAFSYGFF	VIRNAKI	
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mouse	AACI (SEQ ID NO:2)					
rat	AACI (SEQ ID NO:3)					
human	AACI (SEQ ID NO:4)					
chicken	IACI (SEQ ID NO:5)					

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Table 2- FUNCTIONAL PEPTIDE EPITOPES OF HEPARANASE

Peptide	Amino acid sequence	Location in SEQ ID NO 10	Property
p8 #7 SEQ ID NO:7	PAYLRFGGTKTDFLIFDP K	89-107	C-terminus of P8 - Dimerization
pep38 SEQ ID NO:6	CTNTDNPRYK	437-446	located 5 amino acids downstream of a heparin binding site
pep8 SEQ ID NO:8	SWELGNEPNSFLKKA	219-233	contains the proton donor residue of the heparanase active site
pep9 SEQ ID NO:9	RPGKKVWLGETSSAY	334-348	contains the nucleophilic residue of the active site
Pep10 SEQ ID NO:10	TWHHYLNGRTATR	294-307	Designed according to a 3D model as a surface exposed sequence, which bridges substrate binding and active site.

*NOTE: Specific peptide sequences are underlined in the sequence below

*NOTE: Mature heparanase dimer sequences in **bold face**:

MLLRSKPALPPPLMLLLLGLPLSPGALPRPAQAQDVVDLDFFTQEPLH
LVSPSFLSVTIDANLATDPRFLILLGSPKLRTLARGLSPAYLRFGGTKTD
FLIFDPKKESTFEERSYWQSQVNQDICKYGSIPPDVEEKLRLWPYQEQL
 LLREHYQKKFKNSTYSRSSVDVLYTFANCGLDLIFGLNALLRTADLQWN
 SSNAQLLLDYCSSKGYNISWELGNEPNSFLKKADIFINGSQLGEDFIQLH
 KLLRKSTFKNAKLYGPDVGQPRRKTA~~MLKSFLKAGGEVIDSVT~~TWHHYL
NGRTATREDFLNPDVLDIFISSVQKVFQVVESTRPGKKVWLGETSSAYGG
 GAPLLSDTFAAGFMWLDKLGLSARMGIEVVMRQVFFGAGNYHLVDENFDP
 LPDYWLSLLFKKLVGTKVLMASVQGSKRRKLRVYLHCTNTDNPRYKEGDL
 TLYAINLHNVTKYLRLPYPFSNKQVDKYLLRPLGPHGLLSKSVQLNGLTL
 KVVDDQTLPPIMEKPLRPGSSGLPAFSYSFFVIRNAKVAACI (SEQ ID NO:4)

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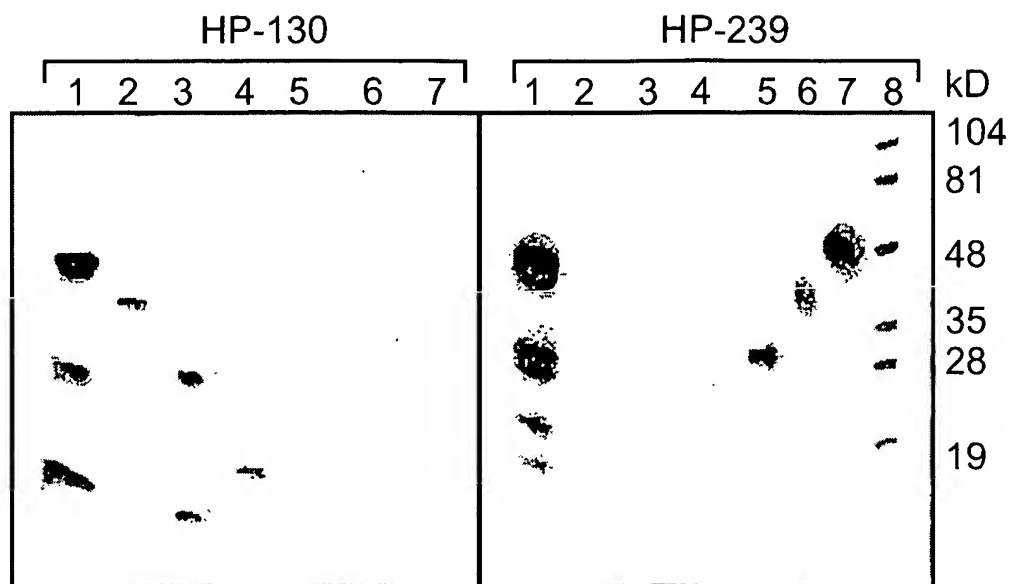


Fig. 1

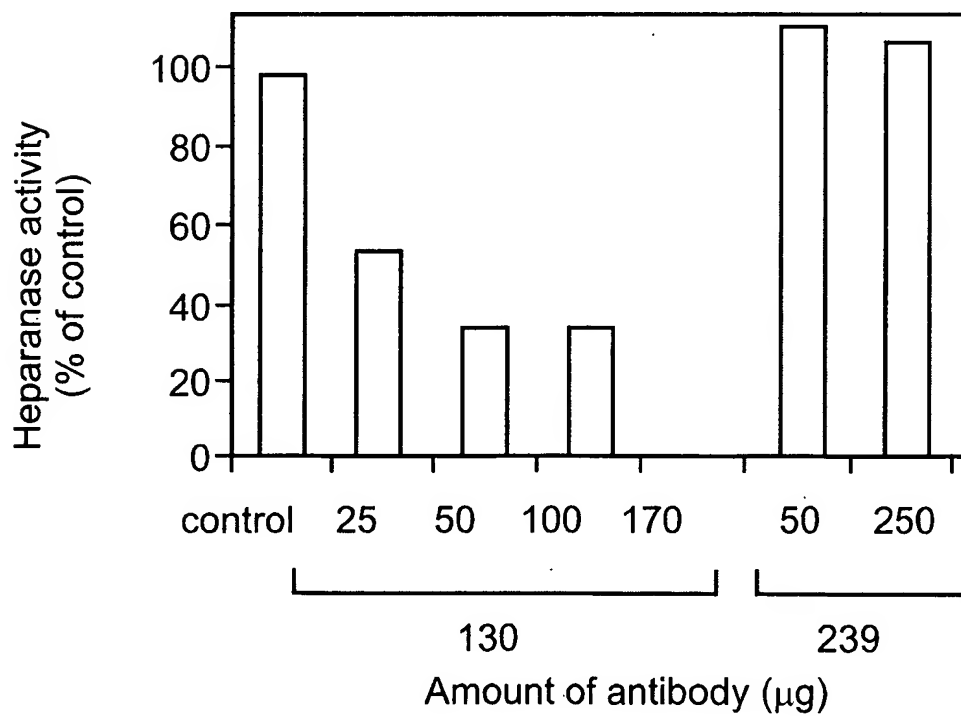


Fig. 2

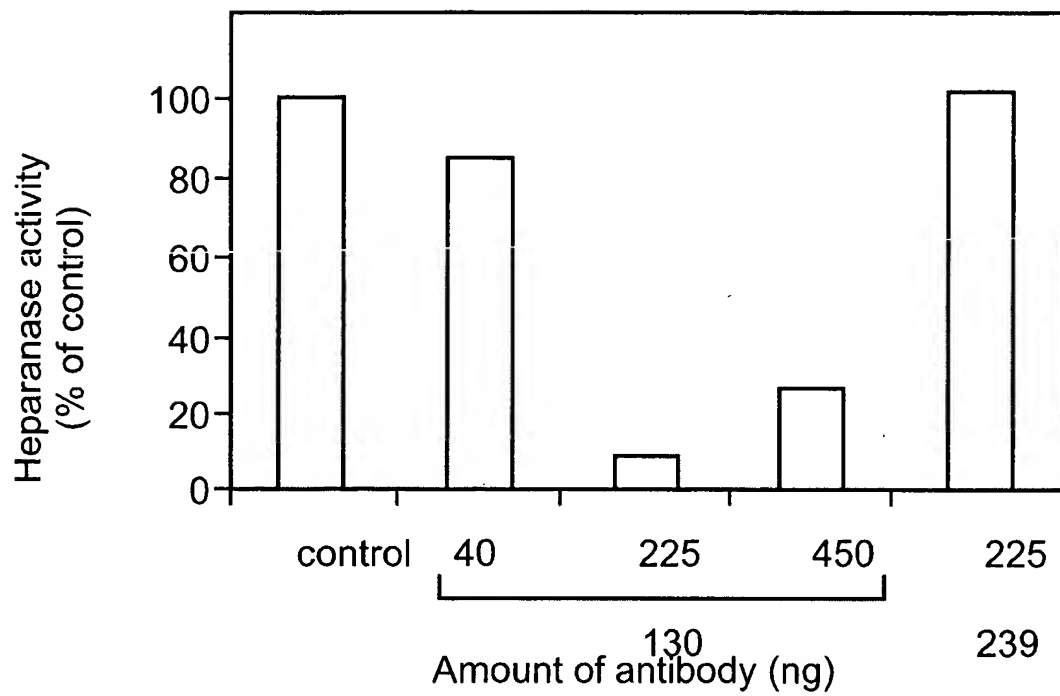


Fig. 3

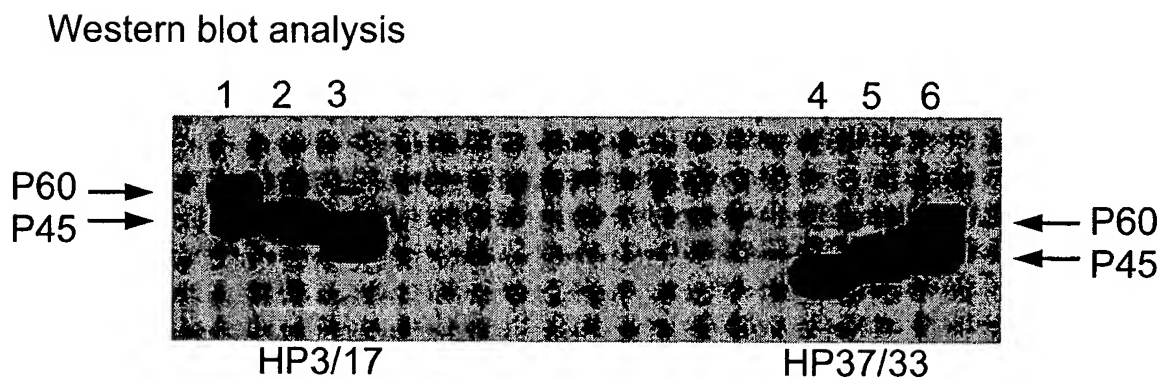


Fig. 4

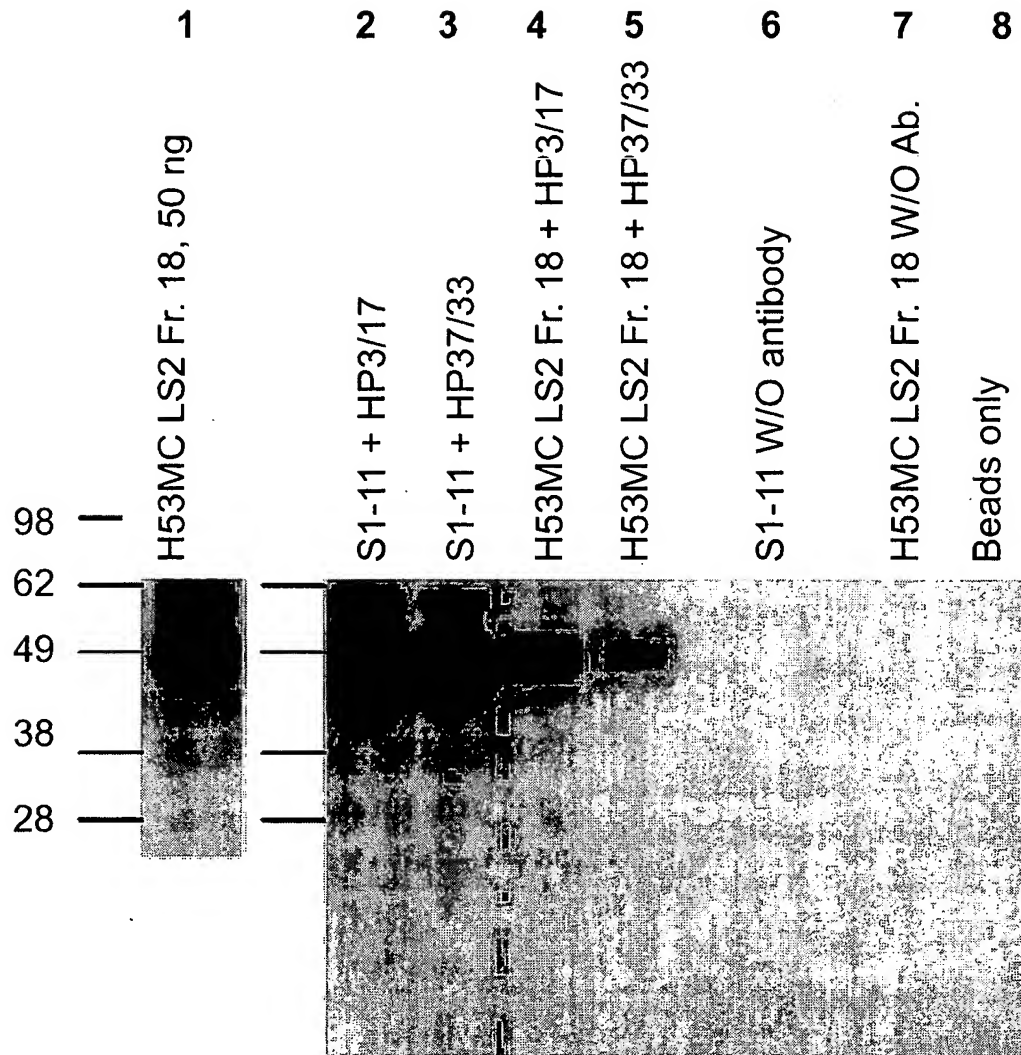
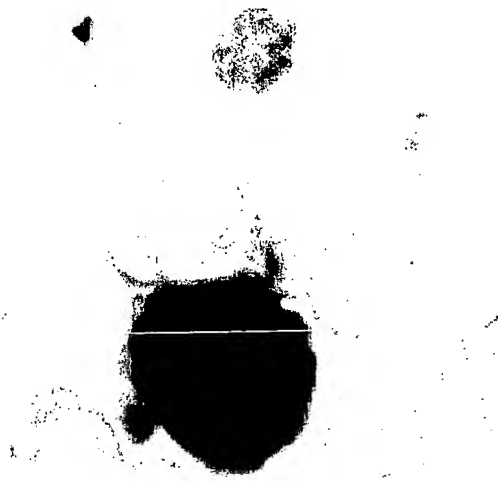


Fig. 5

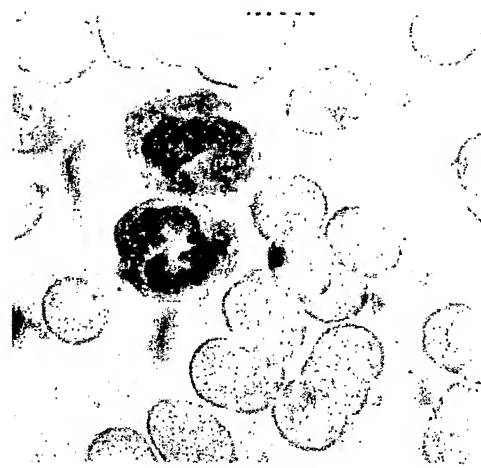
Fig. 6a



Fig. 6b



x 1000



HP37/33

Fig. 6d

Fig. 6c

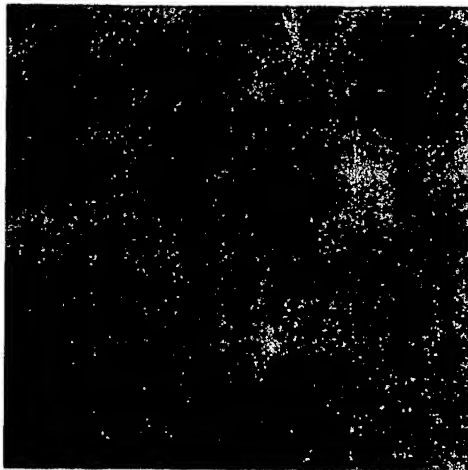


Fig. 7a

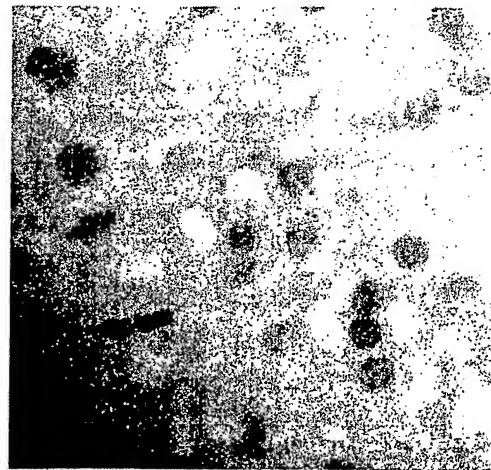


Fig. 7b

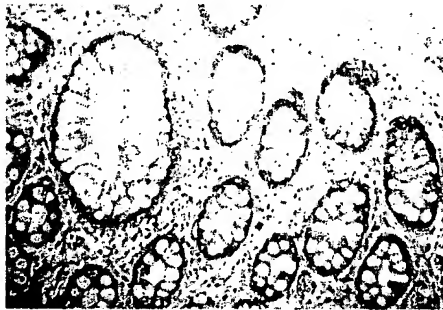


Fig. 8a



Fig. 8b

x 100



x 400

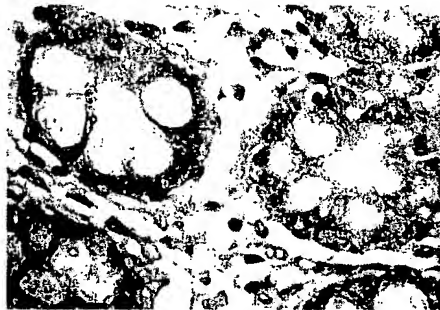


Fig. 9a

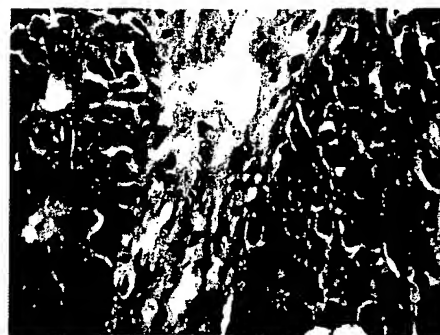
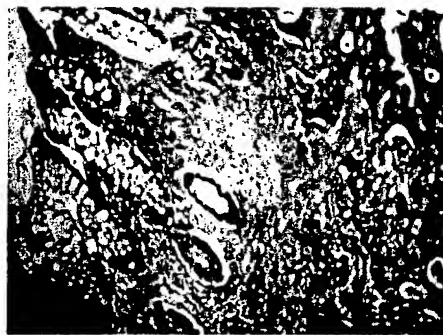


Fig. 9b

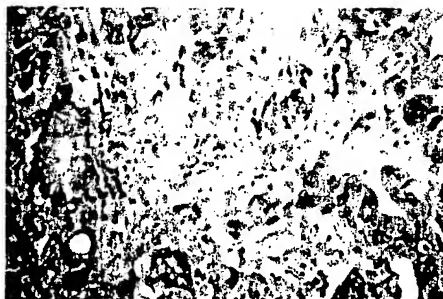


Fig. 9c

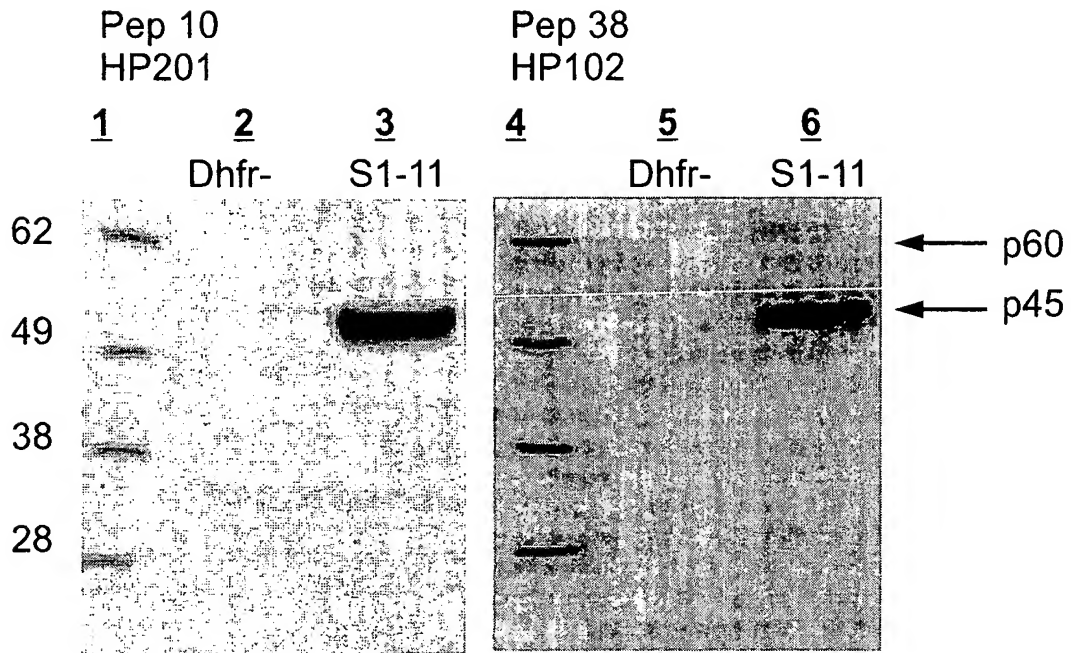


Fig. 10

Results

Group		Day 8	Day 12	Day 15	Day 18
A PBS	Mean	7.8	90.2	375.4	613.6
	SD	12.3	97.7	476.2	859.2
B HP130	Mean	0.0	34.2	188.4	298.2
	SD	0.0	42.8	165.6	111.7
C HP37/33	Mean	0.0	25.3	157.5	229.3
	SD	0.0	29.6	131.2	151.3

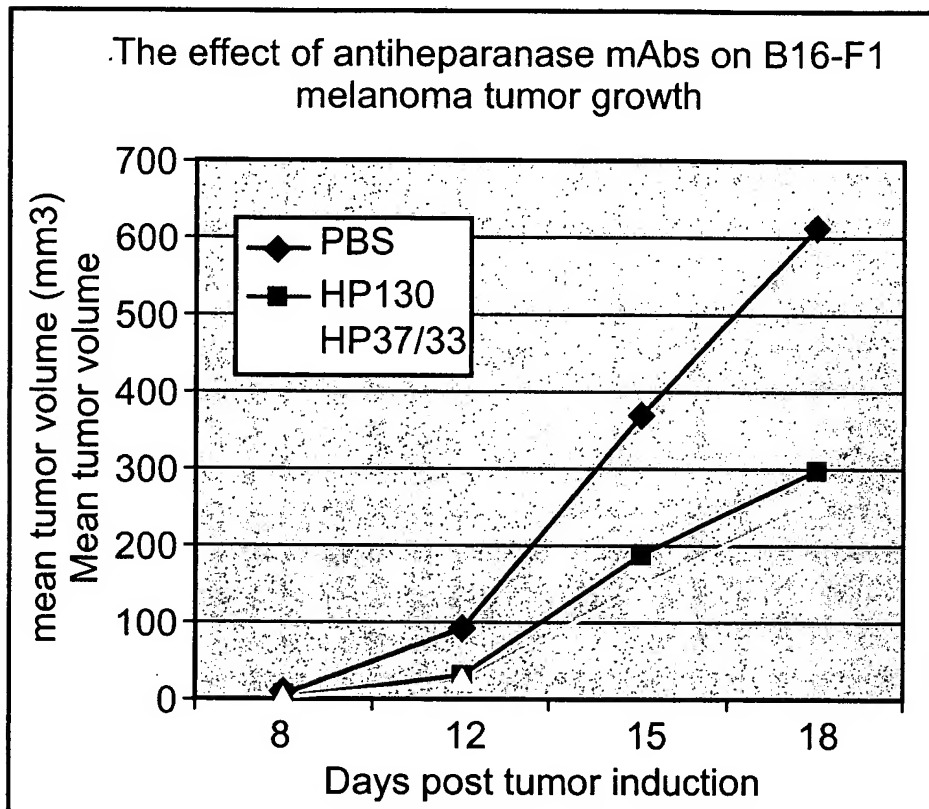


Fig. 11

Group	MEAN ARTHRITIC SCORE (4 legs)		
	Day 7	Day 11	Day 14
A-PBS	4.8	2.4	2.1
B-Mouse a human IgG3	4.9	3.4	2.5
C-HP3/17	4.2	2.1	1.5

Fig. 12

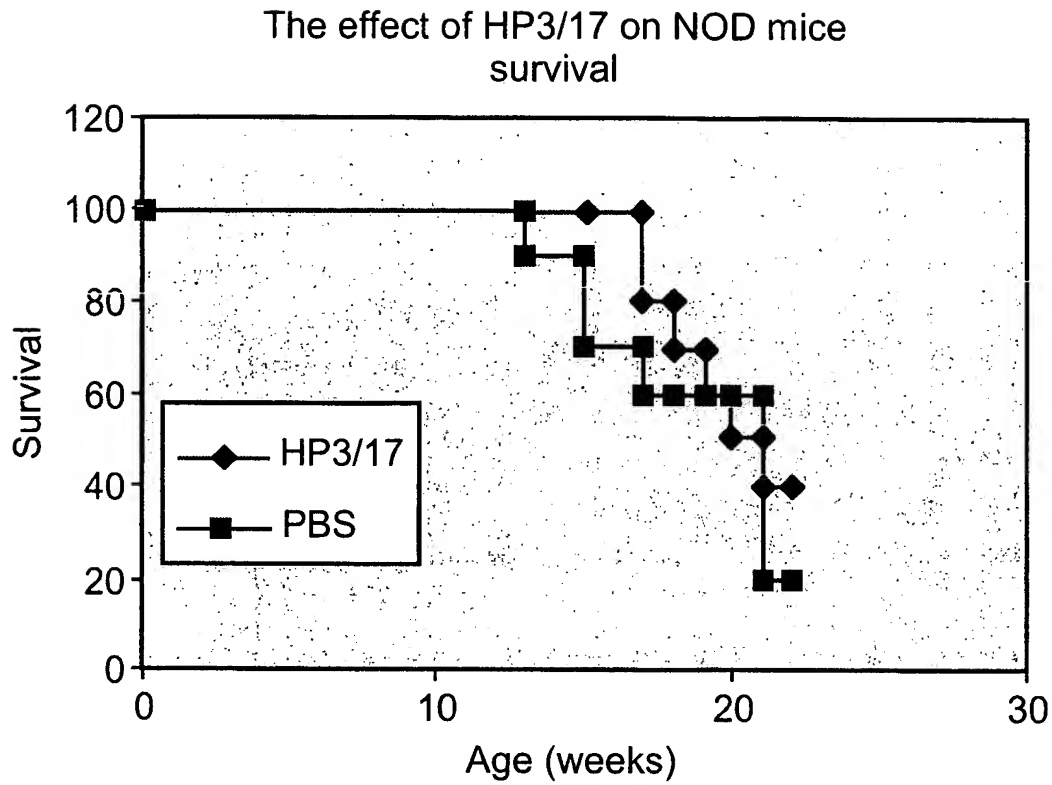


Fig. 13

HP37/33

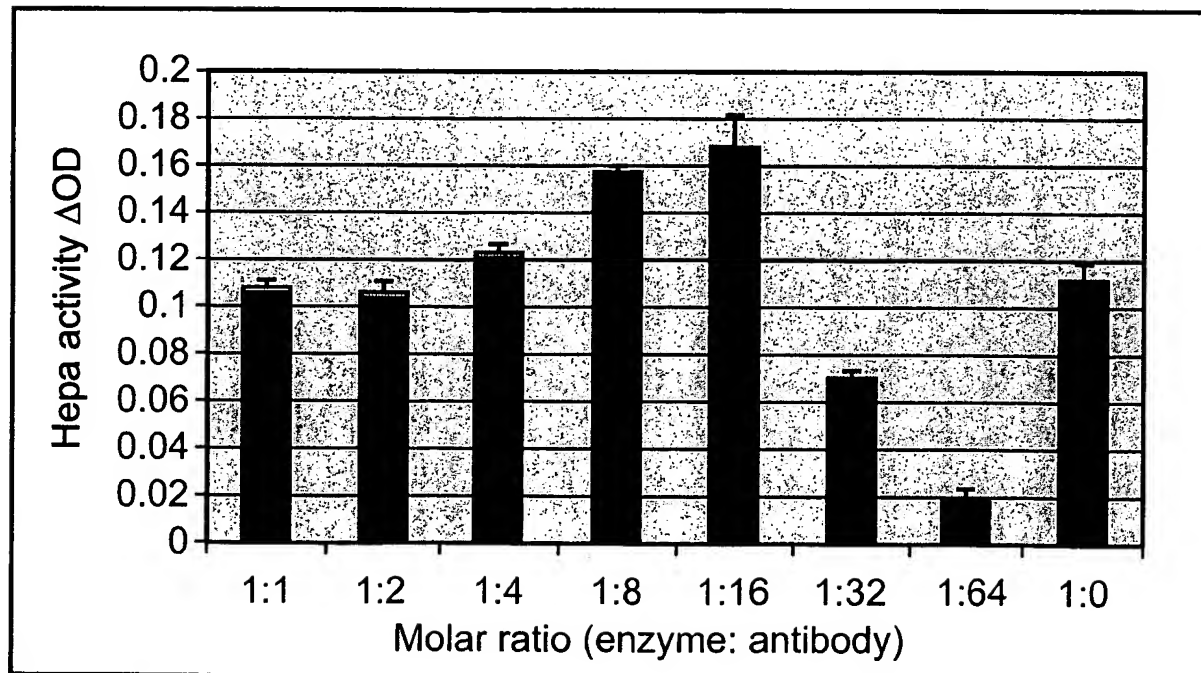


Fig. 14a

HP3/17

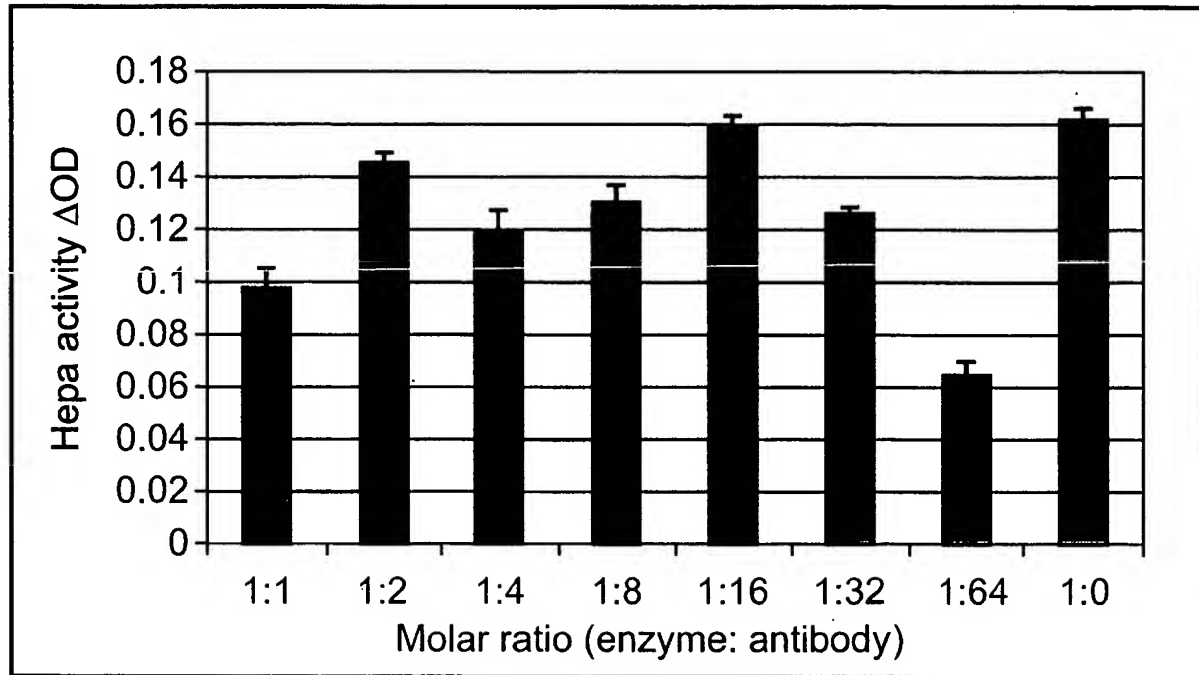
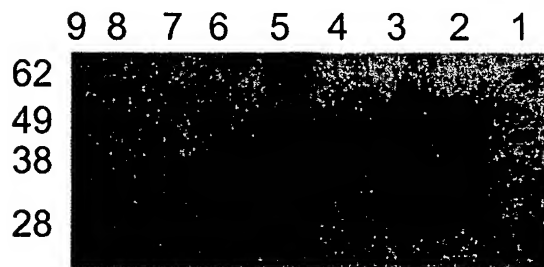
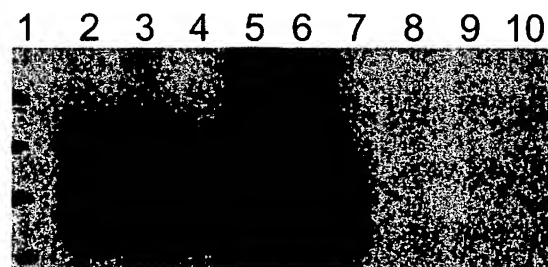


Fig. 14b

Epitope mapping

HP135.108

Fig. 15a



HP37/33

Fig. 15b

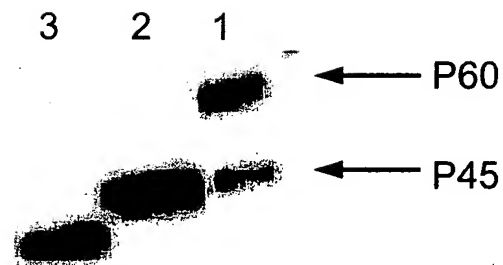
Western blot analysis

Fig. 16

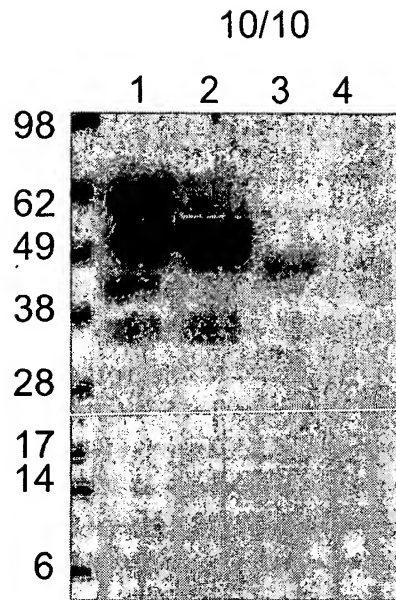


Fig. 17a

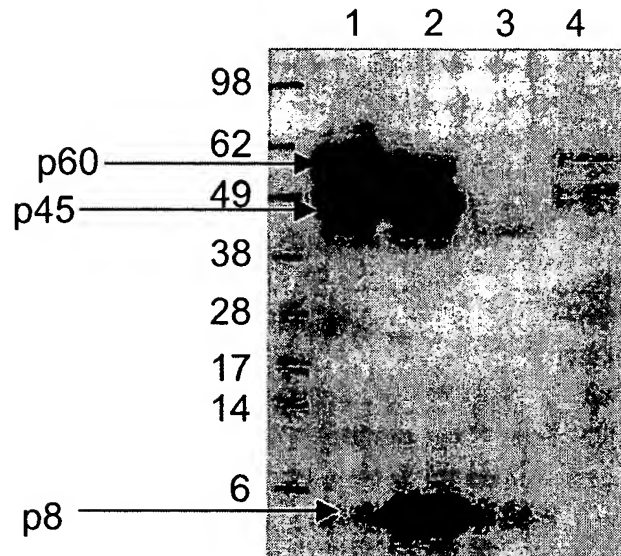


Fig. 17b

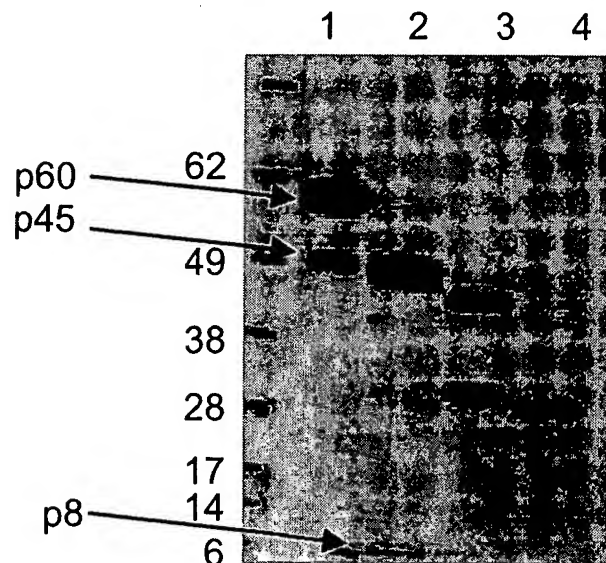


Fig. 17c